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10/510,674	05/23/2005	Bianca Brogmann	Y2428-00162	1884

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DUANE MORRIS LLP - NY
PATENT DEPARTMENT
1540 BROADWAY
NEW YORK, NY 10036-4086

EXAMINER	
JEAN-LOUIS, SAMIRA JM	
ART UNIT	PAPER NUMBER
1617	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,674	BROGMANN ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/18/08, 01/21/09, 03/19/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

This Office Action is in response to the amendment submitted on 03/19/09. Claims 45-58 are currently pending in the application, with claims 1-44 having being cancelled. Accordingly, claims 45-58 are being examined on the merits herein.

Receipt of the aforementioned amended claims, Affidavits, and specification is acknowledged and has been entered.

Applicant's traversal of the Obviousness Double Patenting (ODP) rejection of claims 45 and 47-58 over claims 1-3, 5, 7-8, 11-17, 43-46, and 48-49 of copending Application No. 10/510,673 is acknowledged, but since applicant did not put forth any arguments against this rejection, the ODP rejection is maintained for reasons of record as stated in the previous Office Action and restated below for applicant's convenience.

Applicant's argument that Kaiko does not teach any specific amount or ratios of naloxone except for naltrexone. Applicant further argues that Kaiko contrasts the oral potency of naloxone and naltrexone by stating that naloxone has been reported to be metabolized to an inactive form in its first passage through the liver such that is to be only one fiftieth as potent when parenterally administered whereas other opioid antagonists are retain much of their efficacy.

As a result, applicant argues that if one multiplies ratios of other opioid antagonists by 50, a ratio of 1.85 to 14.8:1 of oxycodone to naltrexone would be taught by Kaiko and not applicant's 2:1 ratio of oxycodone to naloxone. Such arguments are however not found persuasive as the rejection was rendered obvious over a combination of references. Kaiko teaches naloxone as a preferred opioid agonist that can be administered at doses up to 12 mg and even up to 24 mg. Indeed Kaiko does teach that first pass metabolism after oral administration of naloxone reduces its potency which would prompt one of ordinary skill in the art to increase the oral dosage within the effective limit taught by Kaiko (i.e. up to 24 mg) in order to increase the drug's potency. Because Kaiko did not explicitly teach a ratio of oxycodone to naloxone, Patcher was provided to demonstrate that oxycodone and naloxone can be administered in an orally effective amount where one part naloxone is given and 2 to 20 parts of oxycodone is administered. (see Patcher, col. 5, lines 50-64). Consequently, the Examiner contends that one of ordinary skill in the art in view of the disclosure of Patcher would indeed administer the weight ratios of 2-20:1 oxycodone to naloxone with the reasonable expectation of obtaining an orally effective analgesic composition as taught by Patcher. While applicant provided affidavits supporting the notion that a weight ratio of 2:1 exhibit improved bowel function and analgesic properties, the examiner contends that the combined references of Kaiko in view of Patcher would necessarily possess such properties since Patcher does teach the same weight ratio of 2:1 of oxycodone to naloxone. Moreover, the prior art further teach that it is known (as taught by Gordon et al. in

U.S. Patent 4,457,933) that a ratio of 2.5-5:1 parts by weight of oxycodone to naloxone for decreasing oral and parenteral abuse potential of oxycodone. This further supports the notion that one of ordinary skill in the art would have indeed found it obvious to utilize weight ratios similar to the disclosed prior art if the goal was to reduce potential drug abuse of strong analgetic agents. Consequently, the Examiner contends that Kaiko in view of Patcher does indeed render obvious applicant's invention and thus the rejection of record under 35 U.S.C. § 103(a) is maintained.

Applicant's argument that Kaiko was concerned with oral abuse while the disclosure of Patcher was concerned with preventing parenteral abuse of analgesic agents has been considered but is not found persuasive. The Examiner contends that one skilled in the art would have found it obvious to try the oral weight ratio disclosed by Patcher since drug abuse occurs not only via parenteral route but also via oral abuse. Consequently, the Examiner asserts that one skilled in the art for the purpose of averting drug addiction in general would have found it obvious to try the weight ratios of oxycodone to naloxone (i.e. 2:1 ratio) with the reasonable expectation that such ratio would indeed be effective in preventing oral addiction. Thus, the Examiner contends that Kaiko in view of Patcher does indeed render obvious applicant's invention and thus the rejection of claims 45-58 under 35 U.S.C. § 103(a) is maintained.

For the foregoing reasons, the rejection of claims 45-58 under 103 (a) remains proper and is therefore maintained. In view of applicant's amendment, the following ODP, 112, first paragraph and modified 103(a) Final rejections are being made.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In this application, the dosage amount of 10 to about 100 mg of oxycodone are critical or essential to the practice of the invention, however, applicant did not specifically describe such dosages in the claims or in the specification (see specification pg. 17, lines 1-11). While applicant demonstrated a weight ratio of 2:1 using 20 mg of oxycodone to 10 mg of naloxone, nowhere did applicant teach the use of 100 mg of oxycodone to 50 mg of naloxone. Consequently, due to this lack of written description, the weight ratio being claimed by applicant to be used in their composition cannot be fully ascertained.

Provisional Non-Statutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 45 and 47-58 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5, 7-8, 11-17, 43-46, and 48-49 of copending Application No. 10/510,673 (hereinafter Brogmann US Patent Application No. '673). Although the conflicting claims are not completely identical, they are not patentably distinct from each other because both applications are directed to a pharmaceutical formulation comprising a combination of oxycodone and/or its pharmaceutically acceptable salts, and naloxone and/or its pharmaceutically acceptable salts, the combination in a controlled release matrix containing ethylcellulose and at least one fatty alcohol and providing for a sustained release formulation. The claimed invention and co-pending application Brogmann '674 are rendered obvious over another as the claimed invention teaches a subgenus of active agents which include oxycodone and naloxone released from a controlled release matrix whereas Brogmann '674 teaches a broad genus of pharmaceutically active agents that are released from a non-swellable diffusion matrix. Thus, the aforementioned claims of the instant application are substantially overlapping in scope as discussed hereinabove and are prima facie obvious over the cited claims of corresponding application No. 10/510,673.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 45-58 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Kaiko et al. (WO 99/32119, cited by applicant and filed on an IDS 1449) in view of Patcher et al. (U.S. 3,773,955, cited by applicant and filed on an IDS).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of

35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Kaiko et al. teach an oral dosage form comprising a combination of an orally analgesically effective amount of an opioid agonist and an orally active opioid antagonist, the opioid being included in a ratio to the opioid agonist to provide a combination product which is analgesically effective when the combined oral dosage is administered but is aversive in physically dependent subject (instant claim 57; see abstract, pg. 6, lines 28-30, pg. 7, lines 6-8, and pg. 8, lines 5-10). Additionally, Kaiko et al. teach that the dosage forms of the invention cam be provided as a sustained release of the opioid agonist and all of the doses of opioid antagonist via the incorporation of a sustained release carrier into a matrix containing the opioid agonist and antagonist; or via a sustained release coating of a matrix containing the opioid agonist and antagonist (instant claim 45; see pg. 10, lines 6-15 and pg. 23, lines 6-10). As the opioid antagonist, Kaiko et al. teach the use of naloxone, where the amount of naloxone included in the dosage form being large enough to provide an equiantagonistic effect as if naltrexone (i.e. another opioid antagonist) were included in the combination (instant claim 45; see pg. 14, lines 15-18). Moreover, Kaiko et al. teach that small doses of 0.4-0.8 mg of naloxone in man have been found effective to reverse the effects of opioid agonists (instant claim 45; see pg. 13, lines 21-25). As for the opioid analgesics (i.e. agonists) that are useful in the invention, Kaiko et al. teach the use of several agonists, mixed agonist-antagonists, with

oxycodone or pharmaceutically acceptable salts or esters thereof being among the preferred ones that can be administered at an equianalgesic dose of 13.5 mg or a dosages of about 2.5 mg to about 800 mg (instant claims 45-46; see pg. 11, lines 17-20; pg. 15, line 32, pg. 16, lines 11, 15-16 and 23; and pg. 23, lines 17-19). Additionally, Kaiko et al. teach that in the prior art oxycodone-naloxone compositions are known to have a ratio of 2.5-5:1 parts by weight (instant claim 45; see pg. 5, lines 20-22). Moreover, the combination of opioid agonist and opioid antagonist can be employed in admixtures with convention excipients, including carbohydrates or diluents such as lactose (i.e. filler, instant claim 52), magnesium stearate (i.e. lubricant; instant claims 53-54), cornstarch (i.e. flowing agent; instant claim 56; see pg. 19, lines 34-35, pg. 20, lines 5-11, and 19-21; pg. 33, lines 30-32). In the case of oral compositions, the dosage can be provided as tablets, capsules, caplets and gelcaps (instant claim 58; see pg. 9, lines 30-33; pg. 20, lines 14-16). Suitable sustained release formulations and coatings which may be used include the use of alkylcellulose polymers which provide hydrophobic materials including ethylcellulose or aqueous dispersion of ethylcellulose sold commercially as Surelease (instant claims 45 and 49; see pg. 25, lines 8-10 and 22). Other matrix formulations include the use of a controlled release matrix that releases the opioid in a pH-dependent or independent manner and includes the use of hydrophobic materials such as fatty acids and fatty alcohols including stearic acid and stearyl alcohol (instant claims 49-51 and 55; see pg. 30, lines 31-35; pg. 31, lines 8-16; pg. 32, lines 10-13 and lines 25-28; and pg. 33, lines 25-27).

Kaiko et al. do not teach a pharmaceutical preparation containing oxycodone-naloxone with the specific weight ratio of 2:1 or a preparation in the form of specific pharmaceutically acceptable and equally active free base salts.

Patcher et al. teach analgesic composition which does not provide euphoria or physical dependence comprising an oral active dose of naloxone and an oral active strong analgetic in oral dosage form and containing for each analgetic dose of the analgetic agent an amount of naloxone sufficient to negate the euphoretic and dependence producing action of the composition (see abstract, col. 1). Patcher et al. also teach that naloxone is a potent opioid antagonist that can be used in a dose of 0.1-2.5 mg (see col. 2, lines 40-44 and lines 48). Patcher further teaches that potential analgetics that can be used with naloxone include oxycodone that can be provided in a ratio 2-20 parts to 1 (i.e. 2-20 parts oxycodone to 1 part naloxone) to produce an orally effective analgetic composition which does not produce euphoria or physical dependence (instant claim 45; see col. 5, lines 50-54 and 64). Furthermore, Patcher teaches that the naloxone and the analgetic agents used can include all of the pharmaceutically acceptable nontoxic salts including the hydrochlorides, sulfates, bisulfates, tartrates, nitrates, citrates, bitartrates, phosphates, malates, maleates, hydrobromides, hydroiodides, fumarates, succinates and the like (instant claims 47-48; see col. 4, lines 14-22).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to administer the oxycodone-naloxone dosage or particular salts thereof in the formulation of Kaiko et al. in a ratio of 2:1 given that Patcher et al. teach that such ratio provides an effective analgetic composition that negates the euphoria and physical dependence of the composition. Given that Kaiko et al. teach oral dosage sustained release formulation comprising a combination of an orally analgesic effective amount of an opioid agonist and an orally active opioid antagonist provided in a controlled release matrix, and Patcher et al. teach that an analgesic composition of oxycodone to naloxone or salts thereof in a 2:1 ratio is effective in negating euphoria and physical dependence, one of ordinary skill would have been motivated to try such ratio and administer the oxycodone-naloxone or salts thereof in the aforementioned ratio with the reasonable expectation of providing an oral composition that is effective in its analgesic effects but also a composition that negates the euphoric and physical dependence associated with such composition.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory

action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

06/06/2009

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617